CORRESPONDENCE

Correspondents are urged to write briefly so that readers may be offered as wide a selection of letters as possible. So many are now being received that the omission of some is inevitable. Letters should be signed personally by all their authors.

Interactions with Monoamine Oxidase Inhibitors

SIR,—This company receives almost weekly a number of inquiries on the possible hazards to patients and adverse effects of taking certain foodstuffs, drinks, and other drugs while on phenelzine. Despite considerable efforts on our part to disseminate factual information on these aspects of monoamine oxidase inhibitor (MAOI) therapy we are becoming increasingly concerned, as these inquiries show a repeated and continuing misunderstanding of the problem. It would appear that many doctors in general practice and psychiatrists in hospital who actually start a patient on a MAOI drugs have an incomplete appreciation and at times erroneous knowledge of interactions. Their misunderstanding in many instances appears to be based on rather tenuous evidence from a single reported adverse reaction. This interaction is then perpetuated in the literature by succeeding authors who rarely take the trouble to read the original report or substantiate the reaction. In this way the reported interaction acquires unwarranted and unrealistic importance.

The case of bananas is a particularly bizarre example. Saw-Lan Ip in 1966[1] speculated on the possibility of hypertension arising from the pressor effects of the 5-hydroxytryptamine content of bananas but this was never confirmed. However, present fears of adverse reaction appear to stem from one reported case of a hyptensive crisis occurring in a patient who ate whole green bananas stewed in their skins.[2] In fact, while banana skin does contain a fairly high level of tyramine (65 μg/g) the level in the pulp is insignificant.[3] Another constantly recurring example is broad beans. Many patients write to us saying they have been told by their doctor or psychiatrist to avoid eating "beans," no qualification being given as to whether there are French beans, broad beans, baked beans, etc. Even where broad beans are specified it is surprising how few doctors appreciate that only the pods have been shown to constitute a hazard with MAOIs, as the L-poda content lies wholly in the pod. As with banana skins, there must be very few people in the United Kingdom who eat broad-bean pods. Hence two foodstuffs are prohibited to patients when only the skin or pod is the offending item.

The prohibition on alcohol is a constantly recurring point in correspondence, and doctors and patients alike write to us asking how much alcohol can be regarded as safe or what limit of a particular wine or spirit they must not exceed. It is extremely difficult to arbitrate on such a matter, as the interpretation of an "occasional glass" or "a small sherry" can vary from patient to patient. It is now generally accepted that a small intake of sherry, beer, or port consisting of a single glass would be unlikely to present any hazard because of the very low tyramine content of these alcoholic beverages. On the other hand, Chianti should certainly be avoided since a quantity of 400 ml could contain enough tyramine to cause a reaction in a patient taking an MAOI.

With regard to other drugs and MAOIs, areas of popular confusion are those of analgesics and local anaesthetics. Advice is often asked by dental practitioners on the safety of using local anaesthetics incorporating adrenaline or noradrenaline. It was once thought that the effects of these two catecholamines would be potentiated in patients on MAOIs, but it has since been shown that this is not the case.[4] The *British Dental Journal* has stated that "local anaesthetic solutions containing adrenaline or noradrenaline present no special hazard to patients who are taking MAOI antidepressant drugs."[5] Nevertheless it still appears that many doctors and dentists view a dental extraction under local anaesthesia as a potentially hazardous procedure in MAOI patients and warn against it. While it is widely known that pethidine and morphine are contraindicated, there is some uncertainty about the use of alternative analgesics. The fact that narcotic analgesics other than pethidine or morphine may be used with caution by MAOI patients is surprisingly unappreciated.[6]

The danger of adverse and even fatal reactions between MAOIs and foodstuffs appears to be overestimated, no doubt owing to publicity in the lay press when any such misfortunes occur. It may come as a surprise for doctors to learn that only 17 cases of reactions (none fatal) between phenelzine and foodstuffs were reported either to ourselves or to the Adverse Reactions Committee of the Committee on Safety of Medicines between January 1964 and June 1973.[7] Nor has there been reported to us any fatal reaction between phenelzine and a foodstuff since the latter date.

Despite the issue of warning cards on prohibited foods and drugs by the B.M.A., the Association of British Pharmaceutical Industry, the Pharmaceutical Society, and most companies, including ourselves, who manufacture MAOIs a considerable body of medical, quite apart from lay, opinion appears to have an incomplete and at times inaccurate appreciation of the whole food problem with these drugs. We have felt for some time that it would help to disseminate more widely the factual evidence on these hazards if an authoritative statement from some body such as the Committee on Safety of Medicines were to be made setting forth the true facts on interactions between foods or drugs and MAOIs. It would put the whole situation in perspective and would be a valuable contribution to patient safety in MAOI therapy. With this in view I have written to the Committee on Safety of Medicines asking if they could help to clarify the problem where obvious misconceptions presently exist, both authoritatively to inform the doctor and to reassure the patient. They do not feel, however, that they can modify at present the views expressed in their Adverse Reactions Leaflet No. 1, and they think it seems best to avoid publicizing food hazards. While I must agree that to increase the list of possible food hazards may only confuse the situation further and worry patients and doctors more, nevertheless proved reactions must be made known. What is wrong, I believe, is that many published statements on interactions are based on individual reports which represent associations rather than true reactions and to which a causal role cannot always be definitely assigned, and it is these that needlessly increase the uncertainty over MAOI pre-

scribing. Too many clinicians go into print on insufficient evidence when they have a single case. These are taken up and perpetuated by those who write articles on MAOIs as fact. A confused situation is being compounded by inaccurate and misleading evidence where factual and clear authoritative reporting is required for the guidance of both the doctor and the patient. —I am, etc.,

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1 Saw-Lan Ip, F., *Lancet*, 1966, **1**, 91.
2 Blackwell, B., and Taylor, D. C., *British Medical Journal*, 1969, **2**, 381.
3 Boakes, A. J., *Prescribers' Journal*, 1971, **11**, 109.
4 Ellis, J., *et al.*, *British Medical Journal*, 1967, **2**, 75.
5 *British Dental Journal*, 1970, **129**, 60.
6 *British Medical Journal*, 1967, **4**, 284.
7 Committee on Safety of Medicines, *Register of Adverse Reactions*, Vol. 3, January 1964-June 1972.

Screening for Breast Cancer

SIR,—Though a member of the British Breast Group, I asked that my name should not be included among the signatories to the published statement concerning screening for breast cancer (9 August, p. 357). In their statement the members of the group affirmed that they are "convinced that the early diagnosis of breast cancer is important and that it improves the cure rate." I too subscribe to this conviction and, having been involved in the West London pilot study since its inception, I am now also convinced of the reliability of determined mammary screening in the detection of early cancer. Despite all the expected administrative, financial, and staffing difficulties I should like to see a resolute effort made now to establish a national screening service. I had hoped that the British Breast Group would give its co-operative and authoritative blessing to this concept, but that was not to be. A great opportunity may have been lost.

I had accepted that the published statement represented the views of the majority of my colleagues in the group, however, and it was not this that has prompted my reply. The statement by the group may have been unnecessarily cautious, but it was at least factual. The same cannot be said of the ill-considered leading article which appeared in the same issue of the *B.M.J.* (p. 338) and which presumably was stimulated by the statement by the group.

How do you justify the assertion that "it is now evident that purely local treatment by surgery or radiotherapy rarely cures the disease"? Do you mean one or two per thousand treated patients by the use of the word "rarely"? If so, then this is contrary to all the accumulated clinical experience of the past 40 years. If a much larger number is meant, then why use the word "rarely" at all, unless it was done deliberately to mislead?

Just one fact will suffice to give the lie to this particularly unfortunate example of slipshod reporting. Over a 20-year period between 1941 and 1960 the incidence of mammary cancer consistently exceeded the mortality from the disease in New York State by 25 per 100 000 female population (incidence, 55/100 000; mortality 30/100 000).[1] This was at a time when radical local surgery was standard treatment. This disparity between incidence and mortality persists to the present day. Surely if cure was rare these rates would have approximated each other by now. The incidence of the disease has certainly increased recently but not enough to account for the continuing marked difference between annual incidence and mortality.

Thousands of women have been cured and will continue to be cured of mammary cancer by appropriate local surgery and radiotherapy without precipitate resort to highly unpleasant forms of systemic treatment. Thousands will also die from the disease, irrespective of systemic therapy, owing to their cancers being diagnosed too late. There is certainly no room for complacency and that is what screening clinics and improved rates of early diagnosis are all about. Nihilistic comments such as that contained in your leading article help not at all. —I am, etc.,

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1 Ackerman, L. V., and Del Regato, J. A., *Cancer; Diagnosis, Treatment and Prognosis*, 4th edn., p. 832. St. Louis, Mosby, 1970.

*** Differences between incidence and mortality rates, with their inherent inaccuracies, do not give as good an assessment of cure as do careful follow-up studies of patients with the disease in a defined geographical area until their survival curve becomes parallel to that of the normal population.[1] In that reported from Cambridge[2] 81 of 704 patients survived for 20 years. The calculated "cured" group, using an extrapolated actuarial model, was 17·6 ± 1·3%. Even after that time surviving women had 16 times the risk of death from the disease compared with normal women. A "cured" patient, in terms of normal life expectancy, may therefore appear "cured" only because her recurrent disease is slow-growing. In the others, the large majority, dissemination must have taken place at the time of primary treatment. We did not advocate the need for "unpleasant forms" of systemic therapy in these patients but recorded that trials of systemic therapy are under way. We might remind Mr. Burn that radical local therapy is not pleasant or free from morbidity.—ED., *B.M.J.*

1 Easson, E. C., and Russell, M. H., *The Curability of Cancer in Various Sites*. London, Pitman, 1968.
2 Brinkely, D., and Haybittle, J. L., *Lancet*, 1975, 2 95.

Granny-battering

SIR,—Hardly a week goes by without some reference in the national press or medical journals to baby-battering, and I think it is about time that all of us realized that elderly people too are at times deliberately battered. I have personal knowledge of cases in which it has been possible to confirm that elderly patients have been battered by relatives before admission to hospital and in which there has been no doubt that the battering was deliberate. In other cases assault at home has been suspected but could not be confirmed. This leads one to wonder how many of the elderly who "fall down frequently, doctor" do so because they are assaulted.

Often the type of patient in whom the suspicion of battering must be very high has some mental impairment. While in no way condoning the battering of elderly people by their relatives, I am certain it is just another manifestation of the inadequate care we as a profession give to elderly people and to their relatives who are left with the task of coping with them unaided and unsupported by us. It is hardly surprising under these circumstances that the battering becomes almost a natural consequence of the inadequate service. Perhaps general practitioners in particular and casualty officers especially should become as conscious of granny-battering as they are now aware of baby-battering. Community nurses, health visitors, and social workers should also have this aspect of "caring for the elderly" drawn to their attention.—I am, etc.,

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1 Baker, A. A., *Modern Geriatrics*, 1975, **5**, no. 8, p. 20.

The Aflatoxin-Hepatoma-HBAg Story

SIR,—"More on the Aflatoxin-Hepatoma Story" you entitle your leading article (21 June, p. 647): but there is more yet. If aflatoxin (AF) is the paradigm, it is but the tip of the mycohepatotoxin iceberg,[1] which includes other aspergillus metabolites like ochratoxin and sterygmatocystin and their penicillium equivalents, luteoskyrin and others, to name but two mould genera commonly found contaminating stored crops. Nor do you mention other plant hepatotoxins such as pyrrolizidine alkaloids (PA), though one of the papers you quote[2] has shown these to be synergistic with AF in producing cirrhosis and hepatoma in primates. Best known as the putative cause of "bush-tea"-induced veno-occlusive disease, these occur throughout the world in disparate genera,[3] sometimes contaminating grain—for example, senecios in South Africa[4] and Iraq,[5] heliotropiums in Central Asia,[6] or even as pot-herbs, as with the leguminous crotalarias of East Africa.[7] The single-dose interval induction of rat hepatoma by AF that you mention is even more impressive with PA,[8] even delivered via the milk of a nursing mother;[9] for which reason Schoental[10] has suggested examination of traditional herbal "medicines" for pregnancy, parturition, or the newborn.

You mention hepatitis B (HB) antigenaemia accompanying hepatoma yet fail to refer to the extrahepatic component of this state—namely, the defective immune response it bespeaks. This may be due to insult with the same toxin which acts directly on the hepatocyte, simultaneously perhaps with colonization with a virus (HB) not itself cytopathogenic but becoming so only indirectly, by evoking a cell-mediated immune response[11] or, in default of this response, producing the persisting antigenaemia you refer to. But AF itself is immunosuppressive,[12-14] as to a lesser extent are ochratoxin and sterygmatocystin, while the fusarial toxin T2[15] is even more so,[11] halting phytohaemagglutinin-induced lymphocyte transformation in dilutions as low as 1 μg/l or less. Furthermore, lymphocyte abnormalities have been noted in the wake of veno-occlusive disease, both human and experimental.[16] And hepatoma, once established, may be as lymphocyte-inhibitory as other cancers.[17] HB antigenaemia has been reported